Constitutively Active Receptors

File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS A GROUP I					
MSHR_mouse	melanocyte-stimulating hormone MSH	TMII	92 VSIVLETTIIL K	adenylyl cyclase activity/ HEK293, *stably transfected*	(Robbins, Nadeau et al. 1993)
CLASS A GROUP II					
5H1B_human	5-hydroxytryptamine$_{1B}$	C-terminus of IC3	313 RERKATKTLGI K, R, Q	binding of [^{35}S]GTP[S] / CHO-KI	(Pauwels, Gouble et al. 1999)
5H2A_human	5-hydroxytryptamine$_{2A}$	C-terminus of IC3	322 NEQKACKVLGI K	IP production / COS-7	(Egan, Herrick-Davis et al. 1998)
2H2C_rat	5-hydroxytryptamine$_{2C}$	C-terminus of IC3	312 NEDDASKVLGI L	PI hydrolysis / COS-7	(Herrick-Davis, Egan et al. 1997)

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CLASS A GROUP II					
A1AB_human	α_{1B}-adrenergic alpha 1B-AR	TMDI junction between TMDIII and IC2	63 FAIVGNILVIL A 142 CAISIDRYIGV A	IP / COS-7	(Scheer, Fanelli et al. 1997)
A1AB_human	α_{1B}-adrenergic alpha 1B-AR	junction between TMDIII and IC2	143 CAISIDRYIGV K	IP / COS-7	(Scheer, Costa et al. 2000)
A1AB_human	α_{1B}-adrenergic	TMIII carboxyl end of IC3 TMV	128 AVDVLCCTASI F 293 REKKAAKTLGI E 204 EEPFYALFSSLG V	IP / COS-1 IP arachidonic acid release IP / COS-1	(Perez, Hwa et al. 1996) (Hwa, Gaivin et al. 1997)
A1AB_human	α_{1B}-adrenergic	C-terminal IC3	293 SREKKAAKT X=19 different substitutions	PI / COS-7	(Kjelsberg, Cotecchia et al. 1992)
A1AB_human	α_{1B}-adrenergic	C-terminus IC3	288 293 KFSREKKAAKTLGI K H L	PI hydrolysis / rat fibroblast	(Allen, Lefkowitz et al. 1991)
A2AA_human	α_2C10-adrenergic alpha-2AAR	C-terminal IC3 loop	373 (348?) EKRFTFVLAV X=F,A,C,E,K	adenylyl cyclase inhibition / HEK293	(Ren, Kurose et al. 1993)
ACM1_human	muscarinic Hm1 muscarinic acetylcholine M1	C-terminal IC3 loop junction	360 SLVKEKKAARTLS A	PI / HEK(U293)	(Högger, Shockley et al. 1995)
ACM2-human	muscarinic acetylcholine M2	junction of IC3 and TMVI	390 KKVTRTIL↑A 1-4 A inserted	IP production, inhibition of cAMP production / COS-7	(Liu, Blin et al. 1996)

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CLASS A GROUP II					
ACM3_rat	m3 muscarinic (rat) muscarinic acetylcholine M3	TMVI	507 TWTPYNIMVLVNT S	IP / COS-7	(Blüml, Mutschler et al. 1994)
ACM5_human	m5 muscarinic muscarinic acetylcholine M5	N-terminus to TMII TMVI	chimera composed of m2 1-69 m5 77-445 m2 391-466	β-gal / NIH 3T3	(Burstein, Spalding et al. 1996)
ACM5_human	m5 muscarinic muscarinic acetylcholine M5	TMVI	451 459 465 AILLA FIITW TPYNI MVLVST M L H C V S F T	β-gal; radioligand binding / NIH-3T3	(Spalding, Burstein et al. 1998)
ACM5_human	m5 muscarinic muscarinic acetylcholine M5	junction of TMVI and EC3	465 YNIMVLVSTFCDKCV X=V,F,R,K,+more	β-gal; radioligand binding / NIH-3T3	(Spalding, Burstein et al. 1997)
B1AR_human	β_1-adrenergic	C-terminus	389 RKAFQGLLCCA R	adenylyl cyclase; agonist binding / CHW	(Mason, Moore et al. 1999)
B2AR_human	β_2-adrenergic beta-2AR	C-terminal IC3 loop	266 272 FCLKEHKALKTLGI SR K A	adenylyl cyclase activation; agonist binding affinity / COS-7 or CHO	(Samama, Cotecchia et al. 1993); (Lefkowitz, Cotecchia et al. 1993)
DADR_human	dopamine D1A	carboxyl terminal IC3	264 SFKMSFKRETKVLKT I K 288 *from D1B receptor* APDTSIKKETKVLKT	adenylyl cyclase; cAMP accumulation / HEK293	(Charpentier, Jarvie et al. 1996)
DADR_human	dopamine D1	TMVI	286 FVCCWLPFFIL A	CAMP accumulation / COS-7	(Cho, Taylor et al. 1996)
HH2R_rat	histamine H_2	IC2	115 FMISLDRYCAV N,A	cAMP production / HEK-293	(Alewijnse, Timmerman et al. 2000)

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File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS A GROUP III					
OPSD_human	opsin rhodopsin	TMII TMIII TMVII	90 FMVLGGFTSTLY D 113 GCNLEGFFAT Q 292 296 MTIPAFFAKSAAIY E G,E,M ^{292}Ala neutral a.a converted to carboxylate and competes with ^{113}Glu for salt bridge with ^{296}Lys	transducin; phosphorylation by rhodopsin kinase / COS	(Rim and Oprian 1995)
OPSD_human	opsin rhodopsin	TMIII	134 VVLAIERYVVV I,Q,S	transducin; radioligand binding / COS	(Acharya and Karnik 1996)
OPSD_human	opsin rhodopsin	TM6 *plus* TM3	257 RMVIIMVIAFL Y,N *plus* G113Q	transducin, GTPγS uptake / COS	(Han, Smith et al. 1998)
OPSD_human	opsin rhodopsin	TMVII IC2	296 PAFFAKSAAIY G X=E,M natural mutants + 10 different a.a. substitutions disrupts critical salt bridge between ^{296}Lys(TMVII) and ^{113}Glu(TMIII) 134 VVLAIERYVVV Q	transducin; radioligand binding / COS	(Govardhan and Oprian 1994); (Cohen, Yang et al. 19[illegible] (Cohen, Yang et al. 1993)

Figure 1 (Page 4 of 15)

TRFR_mouse	thyrotropin-releasing hormone TRH-R	carboxyl tail	335 FRKLCNCKQK STOP	$^{45}Ca^{2+}$ efflux, $[Ca^{2+}]$ / Xenopus oocytes; IP formation / AtT20, *stably transfected*	(Matus-Leibovitch, Nussenzveig et al. 1995)

Figure **1** (Page 5 of 15)

File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS A GROUP IV					
BRB2_human	bradykinin B_2 B2 bradykinin BK-2	TMIII TMVI	113 AIISMNLYSSI A 256 LLFIICWLPFQI F	IP production / COS-7	(Marie, Koch et al. 1999)

Figure 1 (Page 6 of 15)

File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS A GROUP V					
AG2R_rat	AT_{1A} Type-1A angiotensis II	TMIII	111 ASVSFNLYASV A disrupts ^{111}Asn(TMIII)-^{292}Tyr(TMVII) interaction	phospholipase C; IP production / COS-7	(Groblewski, Maigret et al. 1997)
AG2R_rat	AT_{1A} Type-1A angiotensis II	C-terminus of TM7 other multiple mutations	305 LFYGFLGKKFK Q	IP production / HEK-293; intrcellular Ca^{2+} mobilization / CHO	(Parnot, Bardin et al. 2000)
FMLR_human	formylmethionylleucylphenylalanine (fMLPR)	IC1	51 LVIWVAGFRMTHTVTTISYLNKAVA LVVWVTAFEAKRTINAIWFLNLAVA (K above conflicts with SWISS-PROT database)	PI production; phospholipase C stimulation / COS-7	(Amatruda, Dragas-Graonic et al. 1995)
IL8B_human	interleukin-8 receptor B CXCR-2 chemokine	IC2	138 ACISVDRYLAIVH V	IP production; Ca^{2+} moblization and actin polymerization / NIH 3T3	(Burger, Burger et al. 1999)
LSHR_human	luteinizing hormone (LH)	IC3	564 MATNKDTKIAKK G	cAMP production / HEK293	(Kudo, Osuga et al. 1996)
LSHR_human	luteinizing hormone (LH)	TMVI	578 ILIFTDFTCMA G	cAMP production / COS-7	(Shenker, Laue et al. 1993)
LSHR_human	luteinizing hormone (LH)	TM6	571 577 KIAKKMAILIFTDFTCM I I	cAMP production / COS-7	(Kosugi, Van Dop et al. 1995)
LSHR_rat	luteinizing hormone / human chorionic gonadotropin (LH/hCG)	TMVI	556 ILIFTDFTCMA G, Y	cAMP production / HEK 293T	(Bradbury, Kawate et al. 1997; Bradbury and Menon 1999)
OPRD_mouse	delta opiod receptor	TM3	128 KVLSIDYYNMF A,K,H	adenylyl cyclase inhibition / COS-7	(Cavalli, Babey et al. 1999)
OXYR_human	oxytocin	IC2	137 LMSLDRCLAIC A	IP production / COS-7	(Fanelli, Barbier et al. 1999)

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PAFR_human	platelet-activating factor (PAF)	C-terminus of IC3	231 EVKRRALWMVCTVLAV R	IP production / COS-7	(Parent, Le Gouill et al. 1996)
PAFR_human	platelet-activating factor (PAF)	TMIII	100 CLFFINTYCSV A	arachnidonate release, IP production, adenylyl cylcase inhibition / CHO	(Ishii, Izumi et al. 1997)
PE23_human	prostaglandin E_3, EP3III EP3IV	C-terminal tail	360 FCQEEFWGN FCQMRKRRLREQEEFWGN ↑truncated	inhibition of adenylyl cyclase / CHO-K1	(Jin, Mao et al. 1997)
PE23_mouse	prostaglandin E_3 EP3	carboxyl-terminal tail	336 KILLRKFCQIRDHT (3α) MMNHL (3β) ↑truncated	inhibition of adenylate cyclase / CHO, *stably expressed*	(Hasegawa, Negishi et 1996)
THRR_human	thrombin	EC2 loop	259 268 CHDVLNETLLEGYYAYY DLKD KDF I	$^{45}Ca^{2+}$ efflux, PI hydrolysis, reporter gene induction / COS-7	(Nanevicz, Wang et al. 1996)
TSHR_human	thyrotropin (TSHR) thyroid stimulating hormone	EC1 EC2	486 YYNHAIDWQTG F,M 568 YAKVSICLPMD T	inositol phosphate--diacylglycerol cascade / COS-7	(Parma, Van Sande et al. 1995)
TSHR_human	thyrotropin (TSHR) thyroid stimulating hormone	TMIII TMVII	509 ASELSVYTLTV A 672 YPLNSCANPFL Y	adenylyl cyclase activation / COS-7	(Duprez, Parma et al. 1994)
TSHR_human	thyrotropin (TSHR) thyroid stimulating hormone	TMV	597 VAFVIVCCCHV L	cAMP formation / COS-7 cells	(Esapa, Duprez et al. 1999)
TSHR_human	thyrotropin (TSHR) thyroid stimulating hormone	TMVII	677 CANPFLYAIFT V	cAMP formation / CHO cells	(Russo, Wong et al. 1999)
TSHR_human	thyrotropin (TSHR) thyroid stimulating hormone	IC3	613 621 VRNPQYNPGDKDTKIAK deletion	cAMP formation / COS-7	(Wonerow, Schoneberg et al. 1998)

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TSHR_human	thyrotropin (TSHR) thyroid stimulating hormone	IC3 / TMVI	623 632 KDTKIAKRMAVLIFTDFICM V I	cAMP activation / COS-7	(Paschke, Tonacchera et al. 1994)
V2R_human	vasopressin V2	IC2	136 LAMTLDRHRAI A	cAMP formation / COS-7	(Morin, Cotte et al. 1998)

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File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS B GROUP I					
CALR_human	human calcitonin hCTR-1 hCTR-2	wild type (native) protein		adenylyl cyclase cAMP production / COS-1	(Cohen, Thaw et al. 1997)
CLASS B GROUP II					
PTRR_human	parathyroid hormone PTH / PTH-related peptide	junction of IC1 and TMII junction of IC3 and TMVI	223 TRNYIHMHLFL R,K 410 KLLKSTLVLMP C,others	cAMP accumulation / COS-7	(Schipani, Jensen et al. 1997)
CLASS B GROUP III					
GIPR_human	glucose-dependent insulinotropic peptide (GIP-R)	TMVI	340 VFAPVTEEQAR P	cAMP production / L293	(Tseng and Lin 1997)
GLR_rat	glucagon	junction of IC loop1 and TMII IC end of TMVI	178 TRNYIHGNLFA R 352 RLARSTLTLIP A	cAMP accumulation / COS-7	(Hjorth, Orskov et al. 1998)
VIPR_human	vasoactive intestinal peptide 1 (VIP)	junction of IC loop 1 and TMII junction of IC loop 3 and TMVI	178 RNYIHMHLFI R *requires functional integrity of the N-terminal EC domain* 343 LARSTLLLIP X= K,P	cAMP production / COS-7 or CHO	(Gaudin, Maoret et al. 1998) (Gaudin, Rouyer-Fessard et al. 1998)

Figure 1 (Page 10 of 15)

File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS C					
CASR_human	calcium-sensing	N-terminal EC	TLSFVAQNKIDSLNLDEFCNCSEHI *various substitutions, in multiple combinations*	IP / tsA	(Jensen, Spalding et al. 2000)

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File Name	Receptor	Mutation Site	Sequence	Assay / Cells	Reference
CLASS D					
O74283 RCB2 C. cinereus	pheromone	TM6	229 PLSAYQIYLGT P	heterologous yeast assay	(Olesnicky, Brown et al. 1999)
STE2_yeast	pheromone α-factor	TM6	258 QSLLVPSIIFI LL	*lacZ* reporter gene	(Konopka, Margarit et al. 1996)
STE2_yeast	pheromone α-factor	double mutations TM5 and TM6	223 MSFVLVVKLILAIR C C 247 251 DSFHILLIMSCQSLL CC CC *double mutations* *shaded double mutations*	*lacZ* reporter gene / yeast	(Dube, DeCostanzo et al 2000)
STE3_yeast	pheromone a-factor	IC3	194 DVRDILHCTNS Q	β-galactosidase	(Boone, Davis et al. 1993)
STE2_yeast	pheromone α-factor	TM6	253 258 LIMSCQSLLVPSIIFI L LP	β-galactosidase	(Sommers, Martin et al. 2000)

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Light Emission Induced by the WT CCK-BR vs. a Constitutively Active Mutant

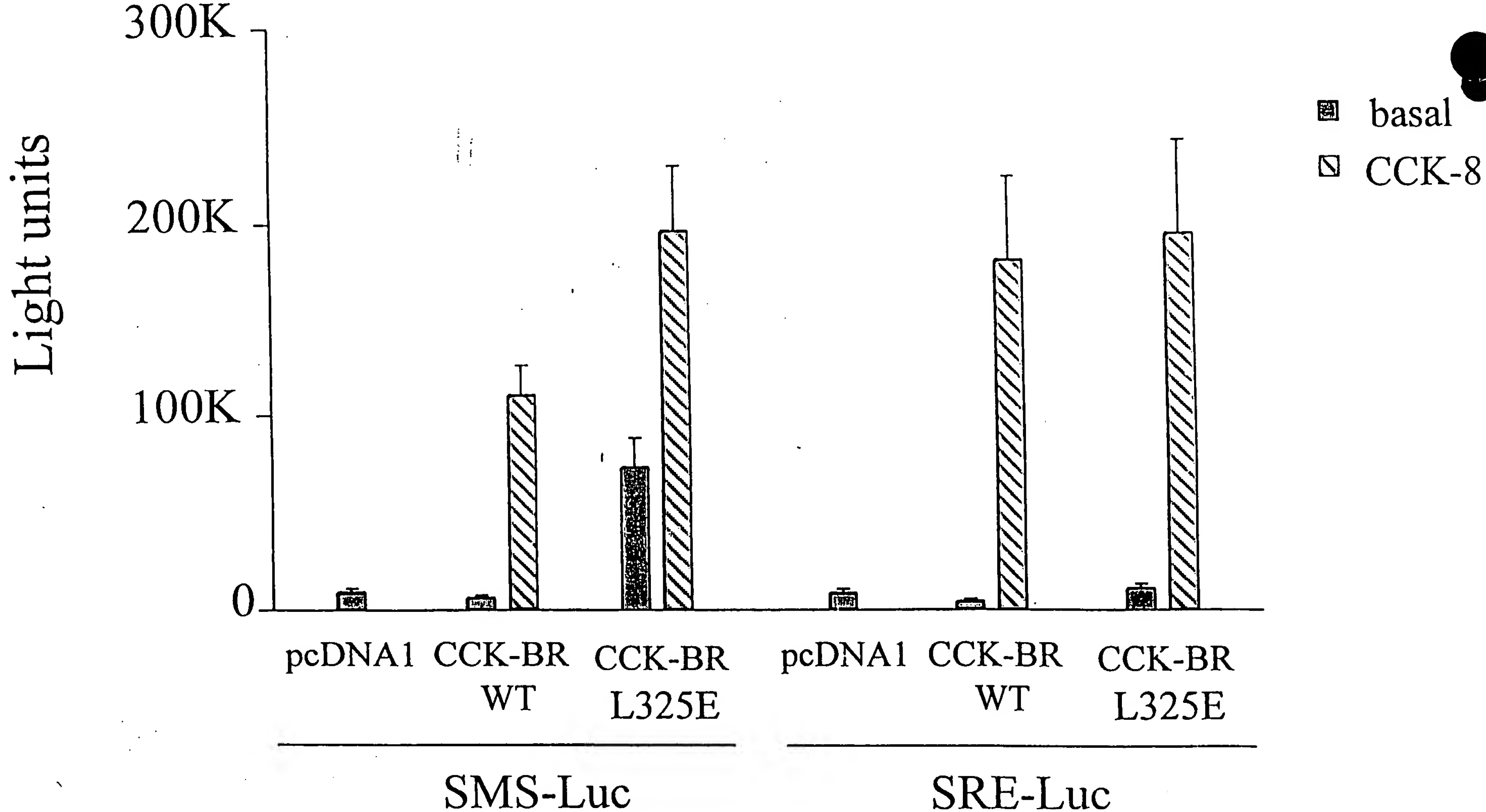


Figure 2

A Point Mutation Confers Constitutive Activity to the Rat μ Opiod Receptor

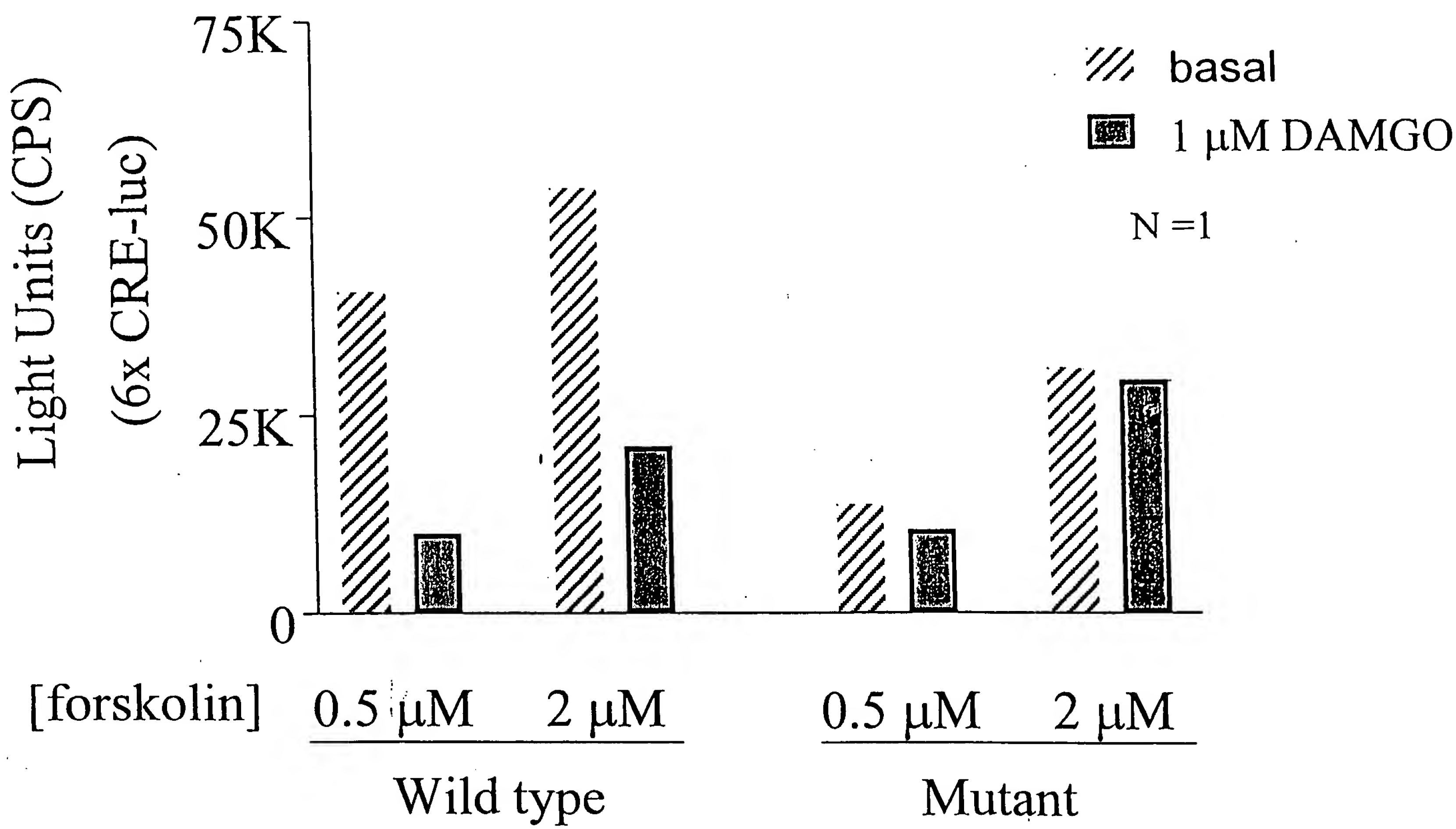


Figure 3

Forskolin Stimulated HEK293 Cells Transfected With pcDNA1 and a CRE-luc Construct

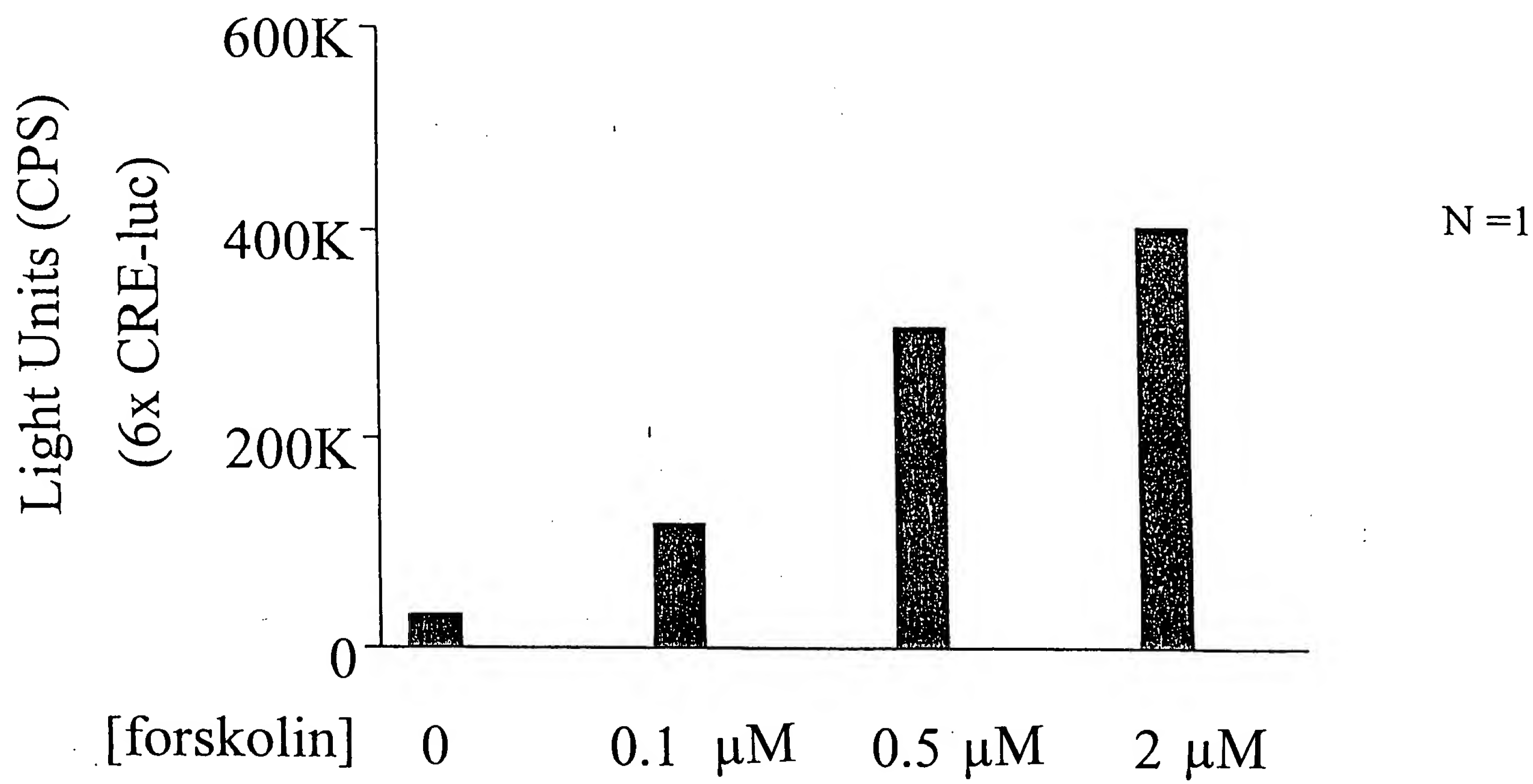


Figure 4

The Rat μ Opioid Receptor Signals Through Gαi

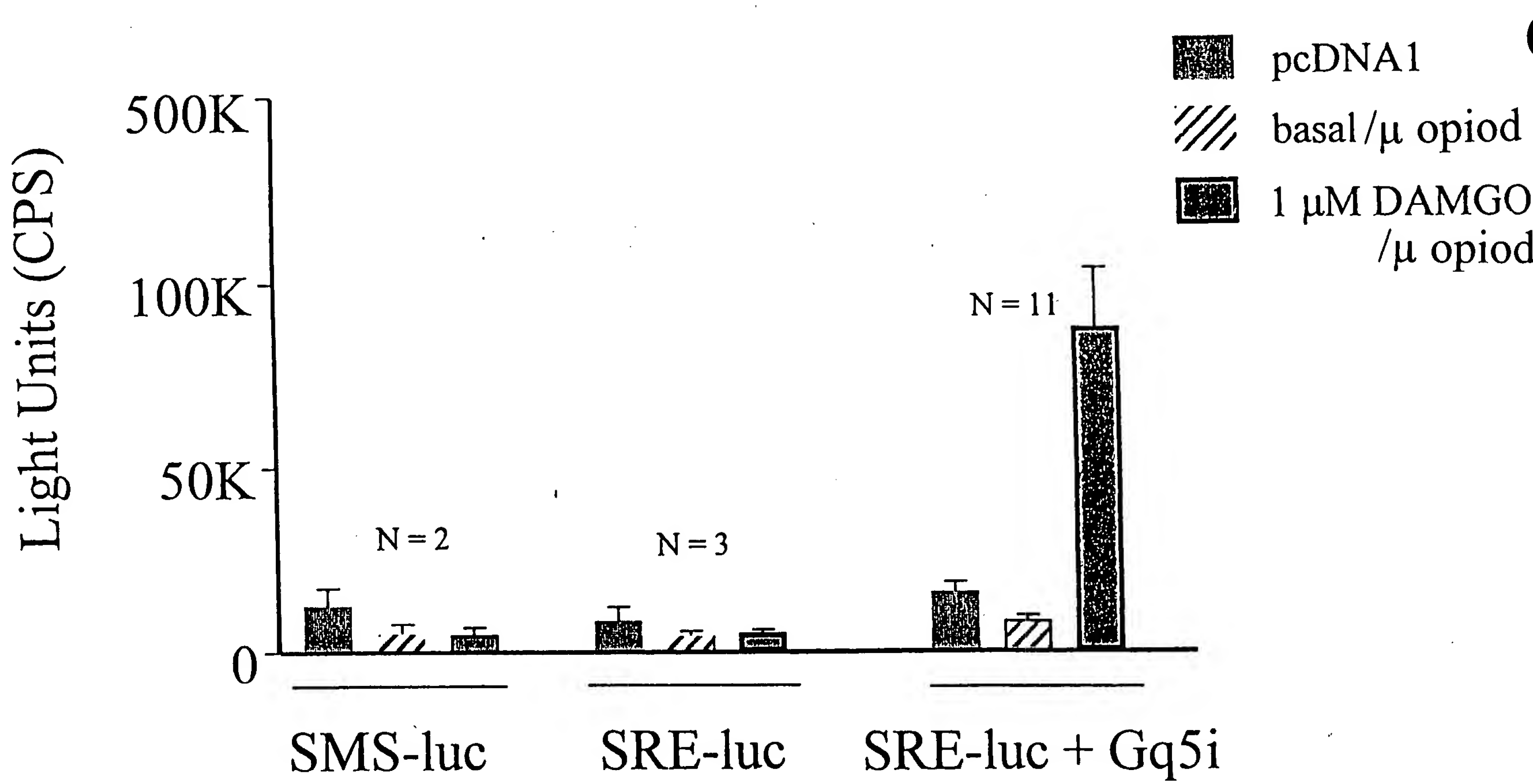


Figure 5

A Point Mutation Confers Constitutive Activity to the Rat μ Opioid Receptor

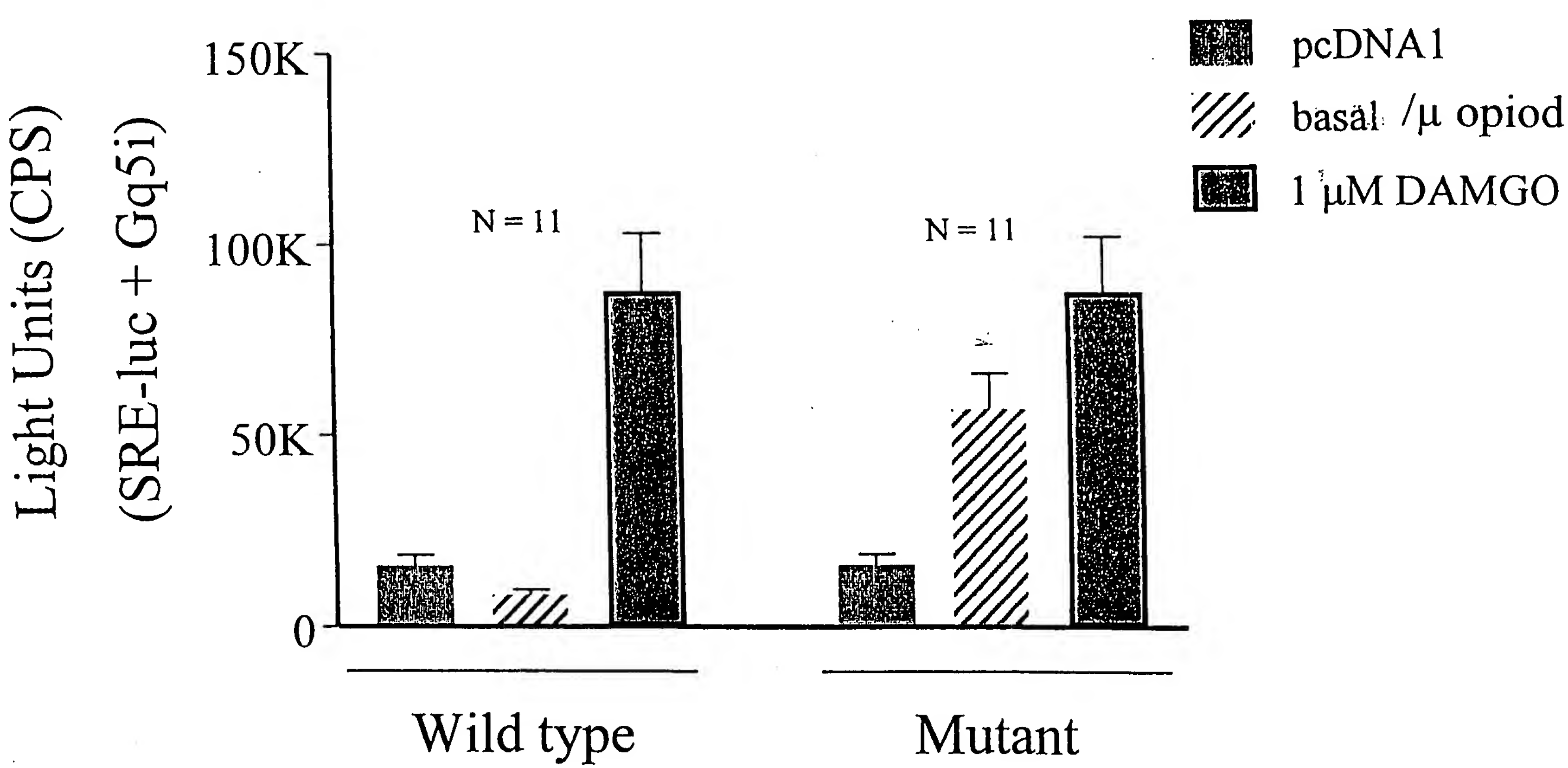


Figure 6

Target Residues Within Class I GPCRs

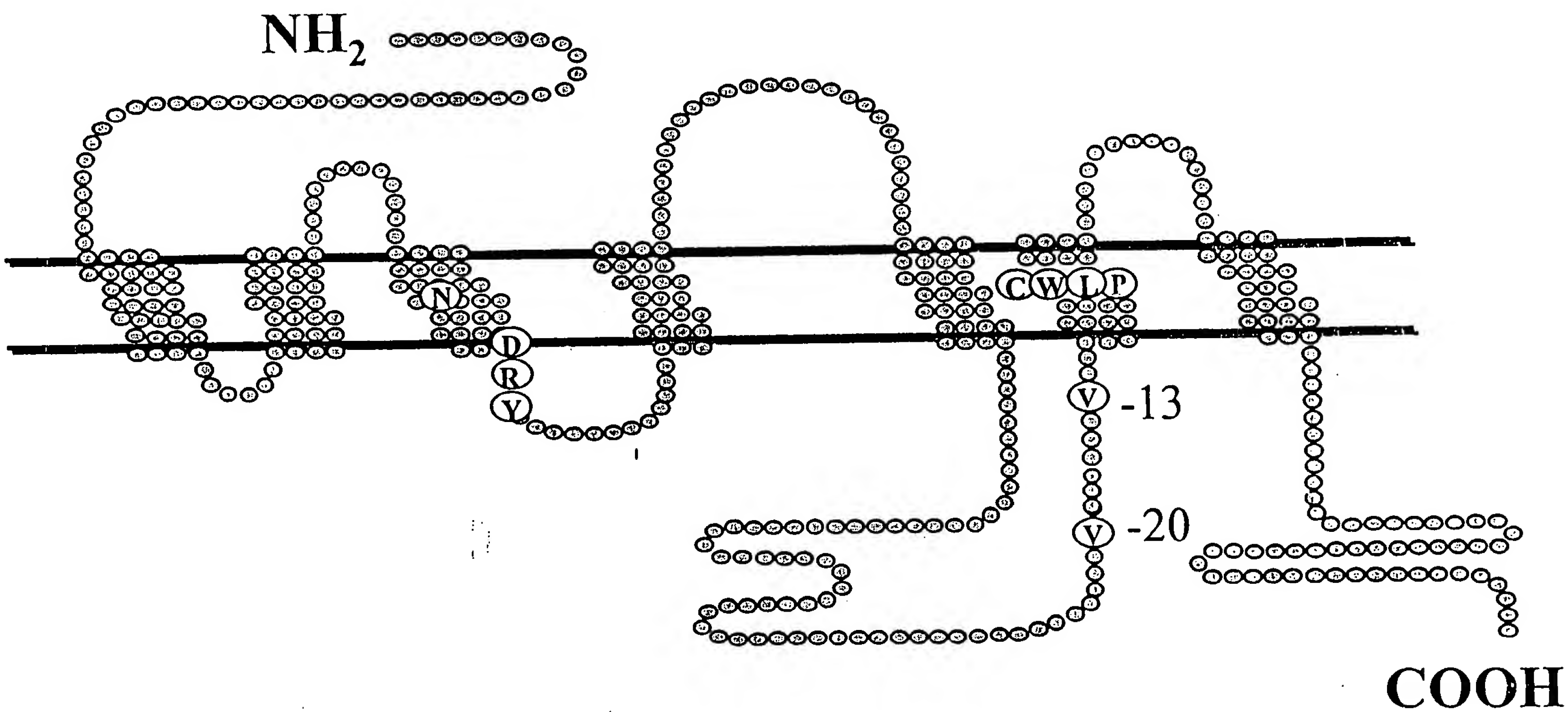
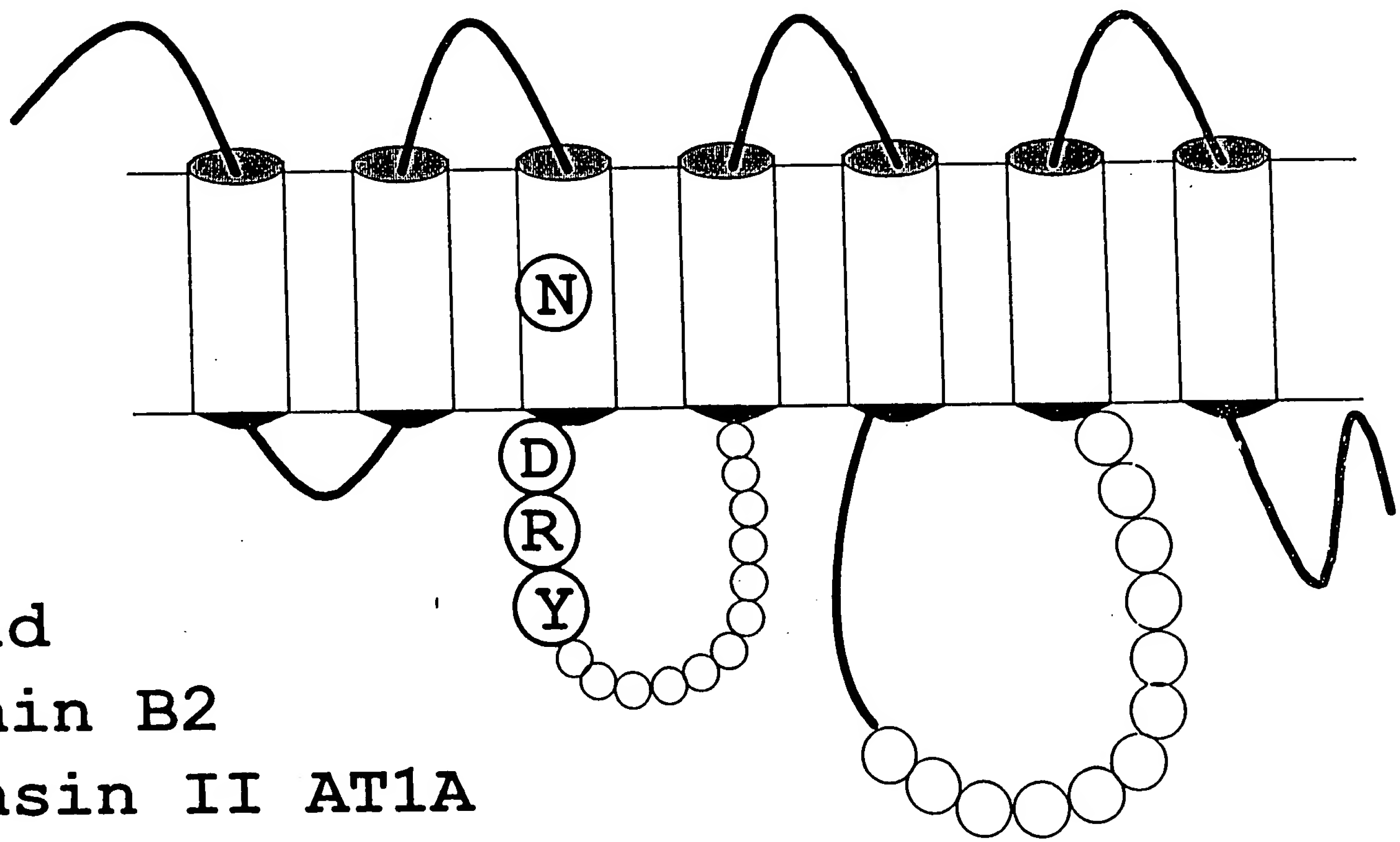


Figure 7

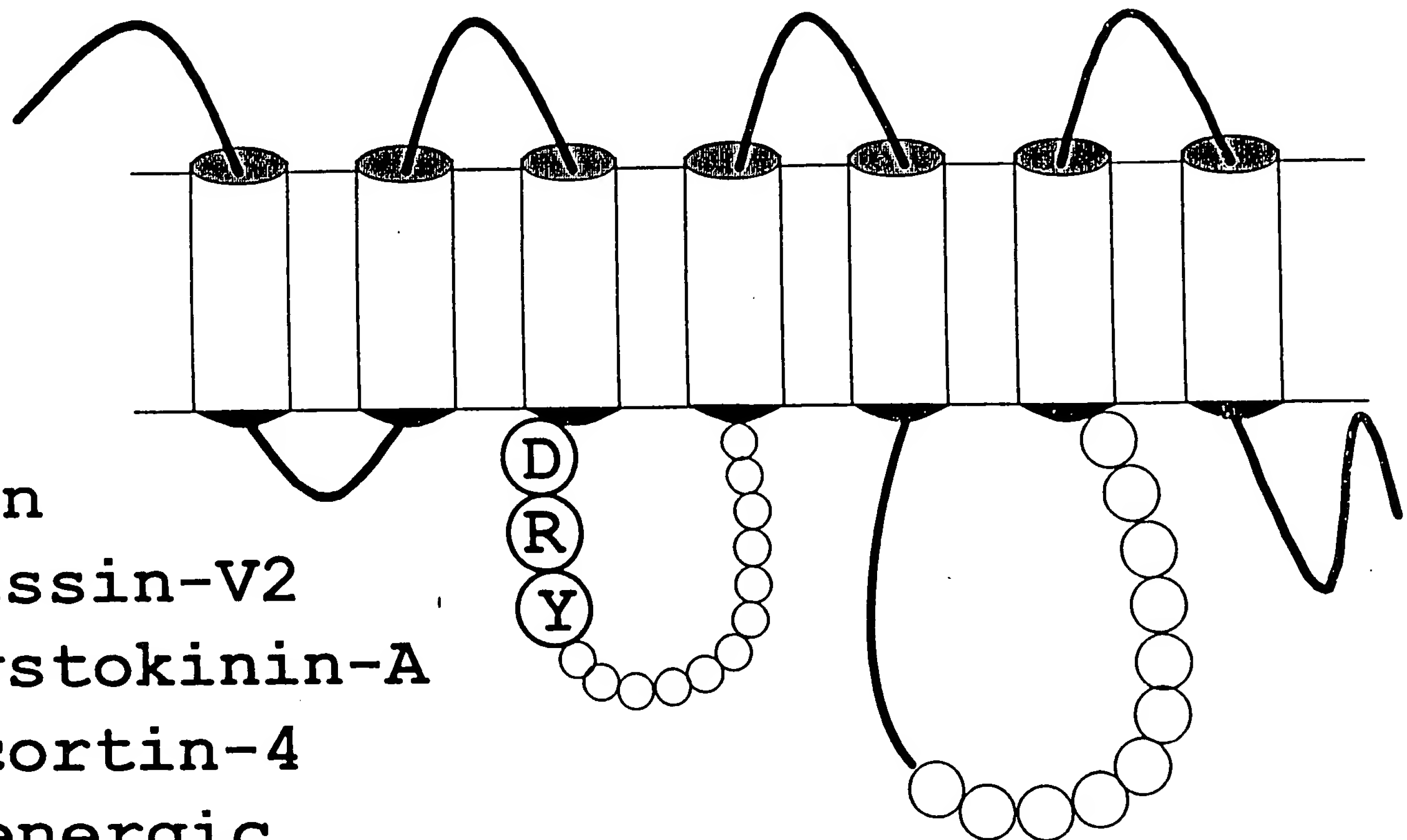
TMD III Asn (-14 from DRY) is a Target for Mutation Induced Constitutive Activity



mu opioid
bradykinin B2
angiotensin II AT1A

Figure 8

The 'DRY' Motif is a Target for Mutation Induced Constitutive Activity



oxytosin
vasopressin-V2
cholecystokinin-A
melanocortin-4
α_{1B} adrenergic

Figure 9

A Point Mutation Enhances MC-4 Receptor Constitutive Activity

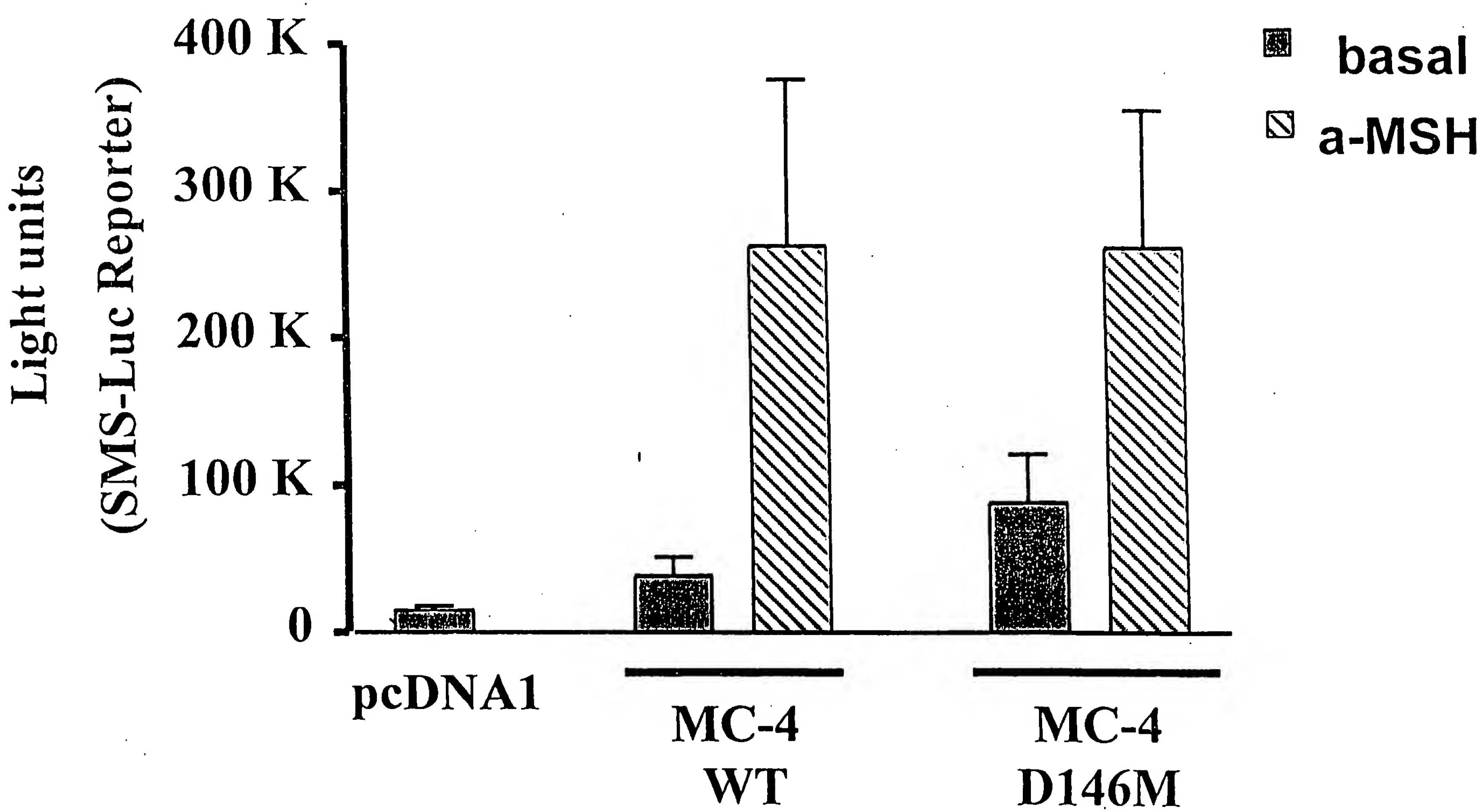
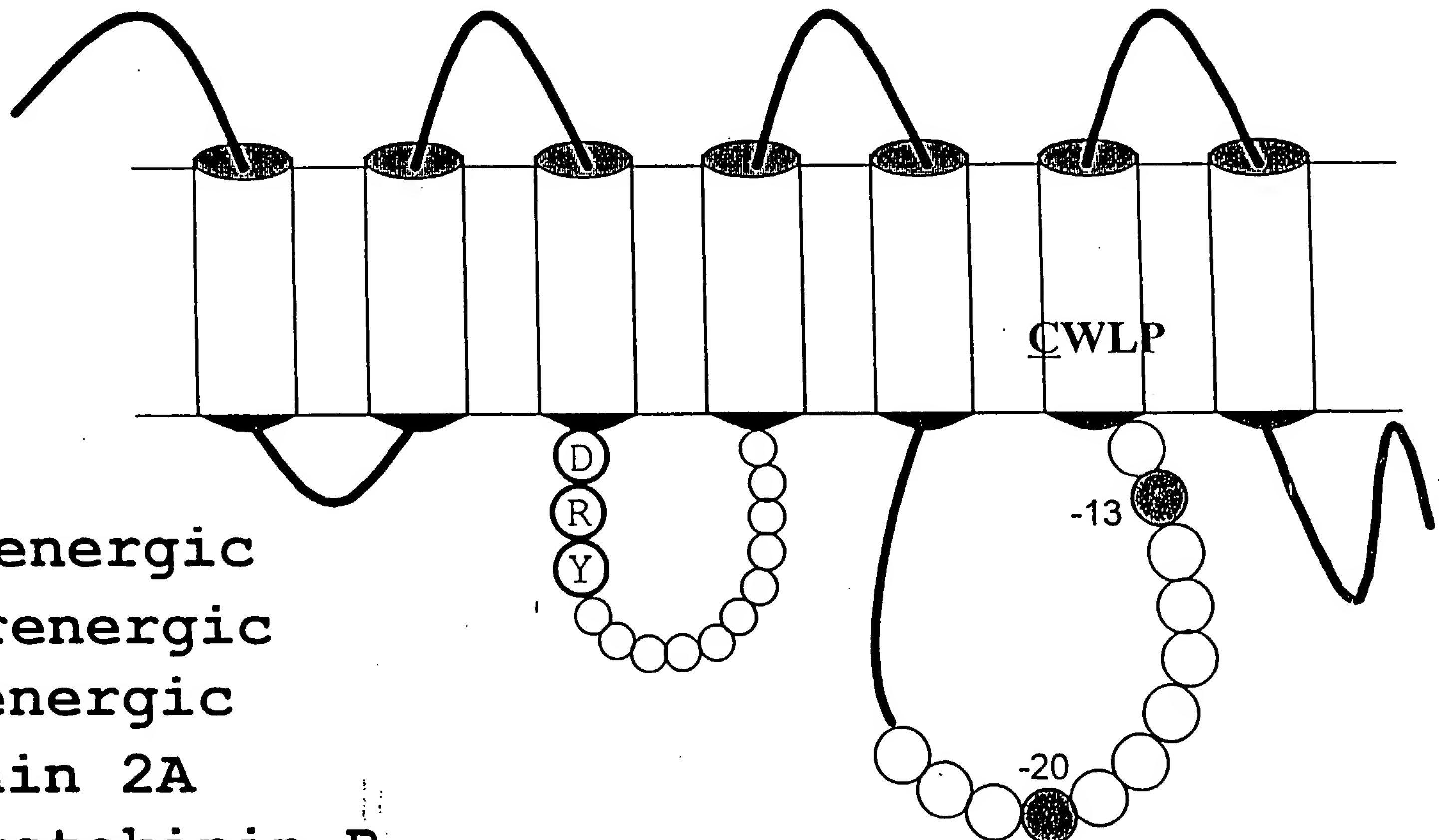


Figure 10

The -13 Position is a Target for Mutation Induced Constitutive Activity



$_{1A}$ adrenergic
α_{2C} adrenergic
β_2 adrenergic
serotonin 2A
cholecystokinin-B
platelet activating factor
thyroid stimulating hormone

Figure 11

```
ork     1 -----------ME[illegible]FRGEPGPTCAPSACLPPNSSAWFPGWAEP.[illegible]NGSAGSEDAQ
crkr    1 -----------MESPIQIFRGEPGPTCAPSACLLPNSSSWFPNWAES..DSNGSVGSEDQQ
orm     1 MDSSAAPTNASNCTDALAYSSCSPAPSPGSWV..NLSHLDGNLSDPCGPNRTDLGGRDSL
ormr    1 MDSSTGPGNTSDCSDPLAQASCSPA..PGSWL..NLSHVDGNQSDPCGLNRTGLGGNDSL
ord     1 ----------------------MEPAPSAGAEL..Q.PPLFANASDAYPSACPSAGANASG
AT1a    1 ------------------------------------------------MALNSSAEDGIKRIQ
BK-2    1 ----------------MFSPWKISMFLSVREDSVPTTASFSADMLNVTLQGPTLNG.TFAQ

ork    49 LEPAHISPAI..PVIITAVYSVVFVVGLVGNSLVMFVIIRYTKMKTATNIYIFNLALADA
orkr   49 LEPAHISPAI..PVIITAVYSVVFVVGLVGNSLVMFVIIRYTKMKTATNIYIFNLALADA
orm    59 CPPTGS.PSMITAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADA
ormr   57 CPQTGS.PSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADA
ord    37 PPGARSASSLALAIAITALYSAVCAVGLLGNVLVMFGIVRYTKMKTATNIYIFNLALADA
AT1a   16 DDCPKAGRHSYIFVMIPTLYSIIFVVGIFGNSLVVIVIYFYMKLKTVASVFLLNLALADL
BK-2   45 SKCPQVEWLGWLNTIQPPFLWVLFVLATLENIFVLSVFCLHKSSCTVAEIYLGNLAAADL

ork   107 LVTTTMPFQSTVYLMN.SWPFGDVLCKIVISIDYYNMFTSIFTLTMMSVDRYIAVCHPVK
orkr  107 LVTTTMPFQSAVYLMN.SWPFGDVLCKIVISIDYYNMFTSIFTLTMMSVDRYIAVCHPVK
orm   118 LATSTLPFQSVNYLMG.TWPFGTILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVK
ormr  116 LATSTLPFQSVNYLMG.TWPFGTILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVK
ord    97 LATSTLPFQSAKYLME.TWPFGELLCKAVLSIDYYNMFTSIFTLTMMSVDRYIAVCHPVK
AT1a   76 CFLLTLPLWAVYTAMEYRWPFGNHLCKIASASVTFNLYASVFLLTCLSIDRYLAIVHPMK
BK-2  105 ILACGLPFWAITISNNFDWLFGETLCRVVNAIISMNLYSSICFLMLVSIDRYLALVKTMS
                                                   -14 from DRY     *

ork   166 ALDFRTPLKAKIINICIWLLSSSVGISAIVLGGTKVR..EDVDVIECSLQFPDDDYSWWD
orkr  166 ALDFRTPLKAKIINICIWLLASSVGISAIVLGGTKVR..EDVDVIECSLQFPDDEYSWWD
orm   177 ALDFRTPRNAKIINVCNWILSSAIGLPVMFMATTKYR..Q..GSIDCTLTFSHPTW.YWE
ormr  175 ALDFRTPRNAKIVNVCNWILSSAIGLPVMFMATTKYR..Q..GSIDCTLTFSHPTW.YWE
ord   156 ALDFRTPAKAKLINICIWVLASGVGVPIMVMAVTRPR..D..GAVVCMLQFPSPSW.YWD
AT1a  136 SRLRRTMLVAKVTCIIIWLMAGLASLPAVIHRNV..YFIENTNITVCAFHYESRN.STLP
BK-2  165 MGRMRGVRWAKLYSLVIWGCTLLLSSPMLVFRTMKEYSDEGHNVTACVISYPS...LIWE

ork   224 LFMKICVFIFAFVIPVLIIIVCYTLMILRLKSVRLLSGSREKDRNLRRITRLVLVVVAVF
orkr  224 LFMKICVFVFAFVIPVLIIIVCYTLMILRLKSVRLLSGSREKDRNLRRITKLVLVVVAVF
orm   232 NLLKICVFIFAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
ormr  230 NLLKICVFIFAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
ord   211 TVTKICVFLFAFVVPILIITVCYGLMLLRLRSVRLLSGSKEKDRSLRRITRMVLVVVGAF
AT1a  193 IGLGLTKNILGFLFPFLIILTSYTLIWKALKKAYEIQKNKPRNDD...IFRIIMAIVLFF
BK-2  222 VFTNMLLNVVGFLLP.LSVITFCTMQIMQVLRNNEMQKFKEIQTE.RRATVLVLVVLLLF

ork   284 VVCWTPIHIFILVEALGS.T.....SHSTAALSSYYFCIALGYTNSSLNPILYAFLDENF
orkr  284 IICWTPIHIFILVEALGS.T.....SHSTAVLSSYYFCIALGYTNSSLNPVLYAFLDENF
orm   292 IVCWTPIHIYVIIKALITIP......ETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
ormr  290 IVCWTPIHIYVIIKALVTIP......ETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
ord   271 VVCWAPIHIFVIVWTLVDID.....RRDPLVVAALHLCIALGYANSSLNPVLYAFLDENF
AT1a  250 FFSWVPHQIFTFLDVLIQLGVIHDCKISDIVDTAMPITICIAYFNNCLNPLFYGFLGKKF
BK-2  280 IICWLPFQISTFLDTLHRLGILSSCQDERIIDVITQIASFMAYSNSCLNPLVYVIVGKRF

                                                              SEQ ID NO:
ork   338 KRCFRDFCFPLKMRMERQSTSRVR.NTVQD.PAYLRDIDGMNKPV-----------  76
orkr  338 KRCFRDFCFPIKMRMERQSTNRVR.NTVQD.PASMRDVGGMNKPV-----------  77
orm   346 KRCFREFCIPTSSNIEQQNSTRIRQNTT.RDHPSTANTVDRTNHQLENLEAETAPLP  78
ormr  344 KRCFREFCIPTSSTIEQQNSTRVRQNTT.REHPSTANTVDRTNHQLENLEAETAPLP  79
ord   326 KRCFRQLCRKPCGRPDPSSFSRAREATARERVTACTPSDGPGGGAAA---------  80
AT1a  310 KKYFLQLLKYIPPKAKSHS...SLSTKM..STLSYRPSDNMSSSAKKPASCFEVE-  81
BK-2  340 RKKSWEVYQGVCQKGGCRSEPIQMENSM..GTL..RTSISVERQIHKLQDWAGSRQ  82
```

Figure 12

```
mORmouse    1  MDSSAGPGNISDCSDPLA.PASCSPA..PGSWLNLSHVDGNQSDPCGPNRTGLGGSHSLC
mORrat      1  MDSSTGPGNTSDCSDPLA.QASCSPA..PGSWLNLSHVDGNQSDPCGLNRTGLGGNDSLC
mORbovin    1  MDSGAVPTNASNCTDPFTHPSSCSPAPSPSSWVNFSHLEGNLSDPCGPNRTELGGSDRLC
mORhuman    1  MDSSAAPTNASNCTDALAY.SSCSPAPSPGSWVNLSHLDGNLSDPCGPNRTDLGGRDSLC
mORpig      1  MDSSADPRNASNCTDPFSPSSMCSPVPSPSSWVNFSHLEGNLSDPCIRNRTELGGSDSLC
mORws       1  MEYS...GNISDFLYPLS.....NEVMS.....NSSVLCRNFSNSTSFLNMNGSSRDSTD
AT1a        1  -----------------------------------------MALNSSAEDGIKRIQDDC
BK-2        1  ------------MFSPWKISMFLSVREDSVPTTASFSADMLNVTLQGPTLNG.TFAQSKC

mORmouse   58  PQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALA
mORrat     58  PQTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALA
mORbovin   61  PSAGSPSMITAIIIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALA
mORhuman   60  PPTGSPSMITAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALA
mORpig     61  PPTGSPSMVTAITIMALYSIVCVVGLFGNFLVMYVIVRYTKMKTATNIYIFNLALADALA
mORws      48  EQDKLP.MIIAIITTLYSIVCVVGLVGNVLVMYVIVRYTKMKTATNIYIFNLALADLCF
AT1a       19  PKAGRHSYIFVMIPTLYSIIFVVGIFGNSLVVIVIYFYMKLKTVASVFLLNLALADLCF
BK-2       48  PQVEWLGWLNTI.QPPFLWVLFVLATLENIFVLSVFCLHKSSCTVAEIYLGNLAAADLIL

mORmouse  118  TSTLPFQSVNYLMG.TWPFGNILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVKAL
mORrat    118  TSTLPFQSVNYLMG.TWPFGTILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVKAL
mORbovin  121  TSTLPFQSVNYLMG.TWPFGTILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVKAL
mORhuman  120  TSTLPFQSVNYLMG.TWPFGTILCKIVISIDYYNMFTSIFTLCTMSVDRYIAVCHPVKAL
mORpig    121  TSTLPFQSVNYLMG.TWPFGTILCKIVISIDYYNMFTSIFTLTTMSTDRYIAVCHPVKAL
mORws     107  TSTLPFQSVNYLMG.TWPFGDVVCKIVMSIDYYNMFTSIFTLTTMSIDRYLAIVHPMKSR
AT1a       78  LLTLPLWAVYTAMEYRWPFGNHLCKIASASVTFNLYASVFLLTCLSIDRYLAIVHPMKSR
BK-2      107  ACGLPFWAITISNNFDWLFGETLCRVVNAIISMNLYSSICFLMLVSIDRYLALVKTMSMG

mORmouse  177  DFRTPRNAKIVNVCNWILSSAIGLPVMFMATTKYRQ.......GSIDCTLTFSHPTWYWE
mORrat    177  DFRTPRNAKIVNVCNWILSSAIGLPVMFMATTKYRQ.......GSIDCTLTFSHPTWYWE
mORbovin  180  DLRTPRNAKIVNICNWILSSAIGLPVMFMATTKYRQ.......GSIDCTLTFSHPTWYWE
mORhuman  179  DFRTPRNAKIINVCNWILSSAIGLPVMFMATTKYRQ.......GSIDCTLTFSHPTWYWE
mORpig    180  DFRTPRNAKIINVCNWILSSAIGLPVMFMATTKYRN.......GSIDCALTFSHPTWYWE
mORws     166  DFRTPRNAKIVNVCNWILSSAIGLPVVVMASTTIENQNSPLQVSNFDCTLLFPHPPWYWE
AT1a      138  LRRTMLVAKVTCIIIWLMAGLASLPAVIHRNV.....YFIENTNITVCAFHYESRNSTLP
BK-2      167  RMRGVRWAKLYSLVIWGCTLLLSSPMLVFRTMK...EYSDEGHNVTACVISYPS..LIWE

mORmouse  230  NLLKICVFIFAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
mORrat    230  NLLKICVFIFAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
mORbovin  233  NLLKICVFIFAFIMPILIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
mORhuman  232  NLLKICVFIFAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
mORpig    233  NLLKICVFIFAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
mORws     226  TLLKICVFILAFIMPVLIITVCYGLMILRLKSVRMLSGSKEKDRNLRRITRMVLVVVAVF
AT1a      193  IGLGLTKNILGFLFPFLIILTSYTLIWKALKKAYEIQKNKPRNDD...IFRIIMAIVLFF
BK-2      222  VFTNMLLNVVGFLLP.LSVITFCTMQIMQVLRNNEMQKFKEIQTE.RRATVLVLVVLLLF

mORmouse  290  IVCWTPIHIYVIIKALITI......PETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
mORrat    290  IVCWTPIHIYVIIKALITI......PETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
mORbovin  293  IVCWTPIHIYVIIKALITI......PETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
mORhuman  292  IVCWTPIHIYVIIKALVTI......PETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
mORpig    293  IVCWTPIHIYVIIKALITI......PETTFQTVSWHFCIALGYTNSCLNPVLYAFLDENF
mORws     286  IICWTPIHIFVIIKALITI......PNSLFQTVTWHFCIALGYTNSCLNPVLYAFLDENF
AT1a      250  .FFSWVPHQIFTFLDVLIQLGVIHDCKISDIVDTAMPITICIAYFNNCLNPLFYGFLGKKF
BK-2      280  IICWLPFQISTFLDTLHRLGILSSCQDERIIDVITQIASFMAYSNSCLNPLVYVIVGKRF

                                                                          SEQ ID NO:
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mORrat    344  KRCFREFC..IPTSSTIEQQNSTRVRQNTREHPSTANTVDRTNHQLENLEAETAPLP    79
mORbovin  347  KRCFREFC..IPTSSTIEQQNSTRIRQNTRDHPSTANTVDRTNHQLENLEAETTPLP    84
mORhuman  346  KRCFREFC..IPTSSNIEQQNSTRIRQNTRDHPSTANTVDRTNHQLENLEAETAPLP    85
mORpig    347  KRCFREFC..IPTSSTIEQQNSARIRQNTRDHPSTANTVDRTNHQLENLEAETAPLP    86
mORws     340  KRCFREFC..IPSPSVIDLQNSTRNSNPQQEGQSSGHKVDRNNRQV-----------    87
AT1a      310  KKYFLQLLKYIPPKAKSHS...SLSTKMSTLSYRPSDNMSSSAKKPASCFEVE----    81
BK-2      340  RKKSWEVYQGVCQKGGCRSEPIQMENSMGTL..RTSISVERQIHKLQDWAGSRQ---    82
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Figure 13